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Recent Evolution of Multiple Resistance of *Blumeria* (*Erysiphe*) *graminis* f.sp. *tritici* to Selected DMI and Morpholine Fungicides in France

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Abstract: Fungicides inhibiting sterol biosynthesis are frequently used for powdery mildew control and can be subdivided into sterol demethylation inhibitors (DMIs) and morpholines with different modes of action. Whereas fungicide resistance to DMIs (*Rdmi*) and morpholines (*Rmor*) has been continuously monitored, there are no data available on the combination of *Rdmi* and *Rmor*, which led us to ask whether multiple resistance to triadimenol (*Rtria*), representing DMIs and to fenpropimorph (*Rfen*), representing the morpholines, evolved in France from 1993 to 1996. The method used allowed testing of both chemicals simultaneously, with the same inoculum. In 1993, the resistance factor of the mean (RFM) of the French wheat mildew population was 9·59 for *Rtria* and 5·11 for *Rfen*. Resistance increased, leading to RFMs of close to 14 for *Rtria* and 8 for *Rfen* at the end of the study. From the analysis of single colony isolates (SCI) that are genetically uniform, the presence of multiple resistance and its increase were evident and in line with the results of bulk isolates. Covariance of resistance to both chemicals was close to one. In contrast to the increase of *Rfen*, the use of morpholines decreased. These effects are supposed to result from multiple selection due to the use of mixtures of DMIs and morpholines that have been favoured in recent years.

Fungicide sensitivity is, in general, not normally but lognormally distributed in a population. A new way to evaluate and describe lognormal data is presented. It is easy and convenient to use and provides solutions for current problems in the literature with lognormal distributions. Multiple resistance, its evolution and persistance are discussed in relation to fungicide use and to implications for anti-resistance strategies. © 1998 Society of Chemical Industry

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Key words: *Erysiphe graminis;* wheat powdery mildew; DMIs; morpholines; multiple resistance; statistics; lognormal

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1 INTRODUCTION

Fungal pathogens continue to have a major deleterious effect on agricultural productivity around the globe.[1] The control of fungi can be seriously reduced through the evolution of fungicide resistance[2,3] that became a particular problem after the application of compounds with specific action and has remained so.[4–6]

The cereal mildews belong to the most important foliar pathogens in France and other parts of Europe and their population genetics has been extensively studied.[7–9] SBI fungicides inhibiting sterol biosynthesis continue to be favoured by farmers for mildew control.[5,6] They can be subdivided into 36 sterol demethylation inhibitors (DMIs) (de Waard, pers. comm. and Reference 10) that inhibit the 14α demethylation, and five so called morpholines (Hollomon, pers. comm. and Reference 11) that mainly inhibit the Δ14 reduction and the Δ7–Δ8 isomerisation.

Resistance to DMIs (*Rdmi*) and to morpholines (*Rmor*) has so far only been described independently from each other in the wheat and the barley mildew pathogens.[5,6,9,12,13] However, a relevant question is in how far *Rdmi* and *Rmor* are combined in the same population and genotype. Such genotypes would be of particular importance, as both groups of chemicals have frequently been used in alternation and even more so as mixtures.

A further point of interest relates to statistics. There is uncertainty in the literature on whether the sensitivity distribution of the genotypes in the population should be treated normally or lognormally and, in the latter case, how data should be presented. Therefore, the main aims of the present investigation of the wheat mildew pathogen, *Blumeria* (*Erysiphe*) *graminis* DC f. sp. *tritici* Marchal, in France were as outlined:[14]

- to analyse the extent of multiple resistance to triadimenol (*Rtria*) representing the DMI group, and to fenpropimorph (*Rfen*) representing the morpholines, as well as its evolution from 1993 to 1996,
- to consider statistical aspects for appropriate evaluation and description of the data and
- to compare the data with the recent regime of fungicide use in the light of anti-resistance strategies.

TABLE 1
Number of Bulk Samples of the Wheat Mildew Pathogen in France from 1993 to 1996 and Their Origin

Year	*France*	*Centre*	*Nord*	*Champagne*	*Bourgogne*	*Bretagne*
1993	94	46	12	24	3	9
1994	59	18	12	21	4	4
1995	21	7	2	8	1	3
1996	15	8	1	2	1	3

2 MATERIALS AND METHODS

Pathogen samples were taken in the middle of March from winter wheat (stage 32 Zadoks scale). Infected leaves, cut at random from untreated fields or plots of known varieties, were put into three or four Petri dishes to allow production of fresh conidia overnight under controlled conditions (17°C, 1000 lux). Number and origin are described in Table 1. For bulk tests, fresh inoculum from each sampling place was transferred to fresh leaves of susceptible cv. 'Pernel' for inoculum production (bulk sample, i.e. mixture of pathogen genotypes). For genotype tests, a single-colony isolate (SCI) was obtained by taking inoculum from an individual colony from 'Pernel' and multiplying separately.

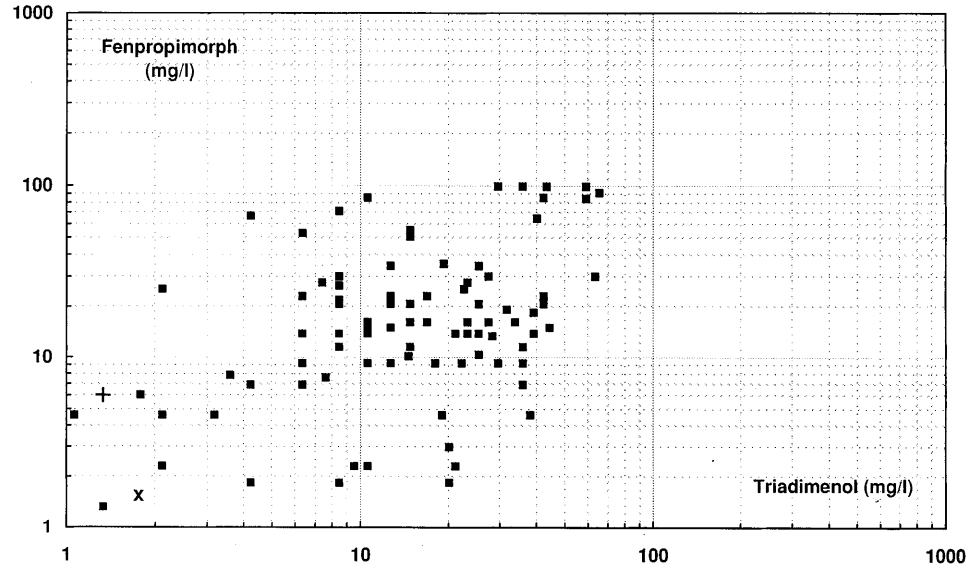

Fig. 1. Sensitivity of the wheat powdery mildew pathogen to triadimenol and fenpropimorph in 1993. Indicated are EC_{50} values of bulk isolates from the main areas of cereal production in the north-west and centre of France (cf. Table 1), and for standard isolates (+) W72 and (×) Be that were obtained from the field before economic use of the respective fungicides.

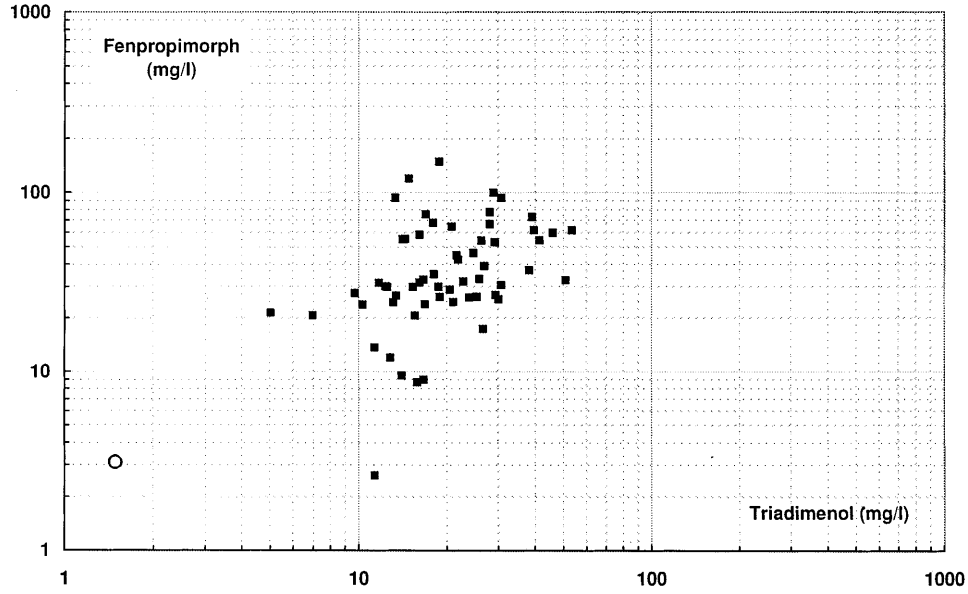

Fig. 2. Sensitivity of the wheat powdery mildew pathogen to triadimenol and fenpropimorph in 1994, compared with (○) the (geometric) mean EC_{50} of the standard isolates. For further description cf. Fig. 1.

Inoculum was ready after one week. Plants were grown under mildew-proof conditions (eight days, 20°C, 15 000 lux during 15 h per day).

Fungicide sensitivity was determined with four replications. Compounds tested were triadimenol 50 g kg^{-1} WP (Bayton 5; Bayer) and fenpropimorph 750 g $litre^{-1}$ EC (Corbel; BASF) kindly provided by the respective manufacturers. Per test, seven wheat pots were used, each containing approximately 35 seedlings. Doses were graded exponentially from 1 to 300 mg $litre^{-1}$ by a factor of $\sqrt{10}$. Fungicides were sprayed in a tower (30 ml per pot) and, to avoid vapour phase interaction, pots were kept separately for 24 h (20°C, 90% relative humidity). Leaf segments (3 cm) were then cut from the middle of primary leaves and placed into one Petri dish per chemical, in a star pattern with increasing doses, starting from the control. For further details of the method see Godet *et al.*[15] The inoculation procedure allowed both fungicides to be tested with the same inoculum. Inoculum density was kept in the range of 200–400 conidia cm^{-2}. After one week at 17°C and 1000 lux, colonies were counted on each segment and the EC_{50} for each test was calculated with an Excel program.

The standard isolates are from fields before application of the respective fungicides, W72 from NIAB Cambridge, UK, Be from Weihenstephan, Germany. They are now used in different European laboratories for monitoring wheat powdery mildew in the network of COST Action 817 (Population studies of airborne

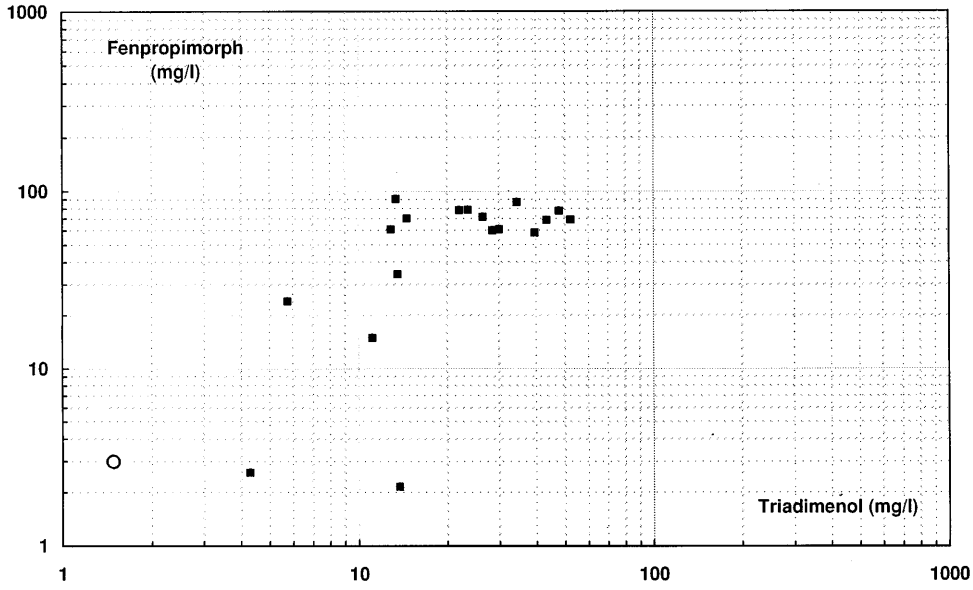

Fig. 3. Sensitivity of the wheat powdery mildew pathogen to triadimenol and fenpropimorph in 1994. Indicated are EC_{50} values of single colony isolates (SCIs) from Département Cher, and (○) the (geometric) mean EC_{50} of the standard isolates.

TABLE 2
Evolution of Fungicide Sensitivity of the Wheat Mildew Pathogen in France from 1993 to 1996 (cf. Table 3)

		EC_{50} (mg litre^{-1})			
		1993	*1994*	*1995*	*1996*
Triadimenol	∅[a]	20·1	21·8	19·2	24·7
	SD[b]	14·7	10·4	13·3	12·0
Fenpropimorph	∅	25·0	43·0	37·5	29·5
	SD	26·4	28·1	19·5	19·0

[a] Arithmetic mean.
[b] Standard deviation, additive, ±, (plus/minus).

TABLE 3
Evolution of Fungicide Sensitivity of the Wheat Mildew Pathogen in France from 1993 to 1996 (cf. Table 2)

		EC_{50} (mg litre^{-1})			
		1993	*1994*	*1995*	*1996*
Triadimenol	∅*[a]	14·70	19·61	13·18	21·42
	SE^*_m[b]	1·09	1·06	1·26	1·16
	SD*[c]	2·38	1·58	2·91	1·78
Fenpropimorph	∅*	15·47	34·77	29·51	23·30
	SE^*_m	1·11	1·09	1·22	1·21
	SD*	2·74	2·01	2·50	2·03

[a] Geometric mean.
[b] Standard error of mean, multiplicative ×/÷ (times/divide).
[c] Standard deviation of entire sample ×/÷.

pathogens on cereals as a means of improving strategies for disease control), and we are grateful to Drs R. Bayles, F. G. Felsenstein and B. Nielsen for providing them. The isolates were included in each test and repeated approximately 50 times per season. In 1994, the standard was not always reliable, probably due to admixtures, and was replaced by new material from the above laboratories. The EC_{50} values for triadimenol and fenpropimorph against W72 were 1·33 and 6·05 mg litre^{-1}, respectively, and against Be, 1·78 and 1·52 mg litre^{-1}, respectively (Fig. 1), giving a mean EC_{50} of the standard of 1·54 mg litre^{-1} for triadimenol and 3·03 mg litre^{-1} for fenpropimorph (Figs 2–4). The resistance factor (RF) was calculated as the EC_{50} of the test isolate divided by the mean of the standard, and the RFM was determined analogously.

For statistical analyses of fungicide sensitivity of populations, means, standard deviations and standard errors of the means were determined. For Table 2, calculations are based on the normal, for Table 3 on the lognormal distribution. In the latter case, instead of giving the two parameters, the mean (∅) and the standard deviation (SD) as logarithms, we transform them into the corresponding antilogs, ∅* and SD*. ∅* then corresponds to the geometric mean, and SD* is a factor of standard deviation that needs to be applied multiplicatively.

3 RESULTS

The sensitivity of the wheat mildew pathogen to triadimenol and fenpropimorph was monitored from 1993 to 1996 in the main areas of cereal production in northwest and central France. The origin of samples is described in Table 1. The graphical presentation of results (Figs 1–4) is mainly given as a comparison between the two fungicides, with sensitivity to triadimenol given on the abscissae.

Our analysis started with the study of 94 bulk isolates in 1993, the sensitivity distribution of which is given in Fig. 1. The (geometric) mean was 14·7 mg litre^{-1} for

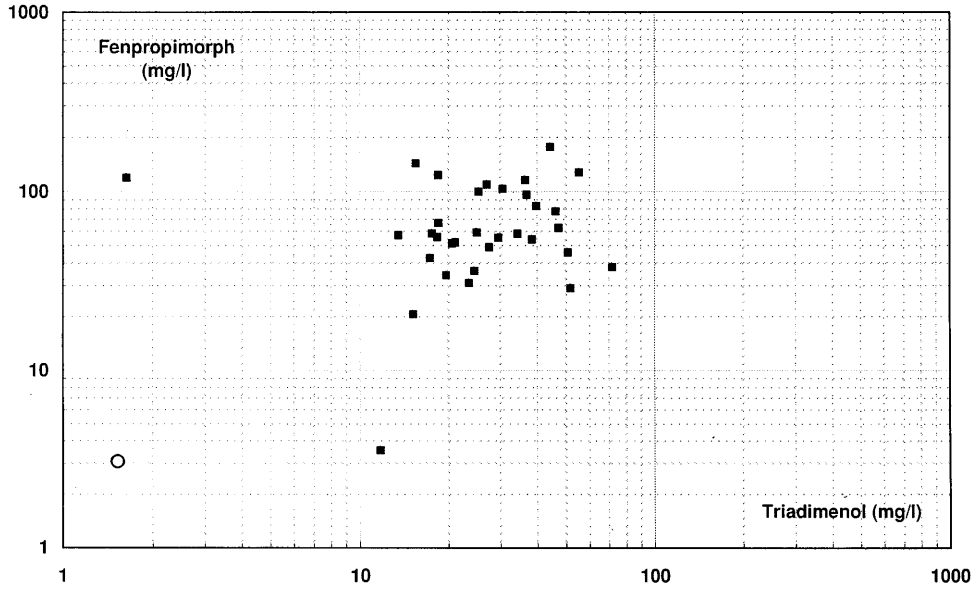

Fig. 4. Sensitivity of the wheat powdery mildew pathogen to triadimenol and fenpropimorph in 1996. Indicated are EC_{50} values of single colony isolates from Département Cher, and (○) the mean EC_{50} of the standard isolates.

triadimenol and 15·47 mg litre^{-1} for fenpropimorph (Table 3). Compared with the mean sensitivities of the standard isolates, 1·54 for triadimenol and 3·03 for fenpropimorph, the resistance factor of the mean (RFM) of the French population in 1993 was 9·59 to triadimenol and 5·11 to fenpropimorph. In comparison, in 1994 the sensitivity of the isolates was considerably more homogenous and closer to their mean EC_{50}, which was significantly higher, at 19·61 mg litre^{-1} for triadimenol and 34·77 mg litre^{-1} for fenpropimorph (Fig. 2). Over the period of three years, mean sensitivities to both chemicals increased by a factor of close to 1·5, and led to RFMs of close to 14 for *Rtria* and 8 for *Rfen* at the end of the investigation (Table 3). The same trend is also obvious from the arithmetic means given in Table 2.

From 1994, we changed our emphasis to allow analysis of single colony isolates (SCIs) from selected areas, as SCIs are genetically uniform and able to inform directly on the genotype of the isolates. The composition of the population from Département Cher was analysed in 1994 and 1996. In 1994, most of the SCIs had an elevated but similar level of resistance to fenpropimorph, combined with an elevated, though more variable level of resistance to triadimenol (Fig. 3). Besides the group of SCIs in the top centre of the figure, however, about one-third was considerably less resistant to both chemicals in 1994. In comparison, in 1996 the group in the top centre was significantly more pronounced in relation to the remainder of the sample, comprising 33 SCIs in total. The small number of isolates sensitive to one or the other chemical are supposed to have remained from close or distant fields or areas with lack of corresponding selection.

Tables 2 and 3 compare different ways of describing population data on fungicide sensitivity. In Table 2, the arithmetic means and standard deviations (additive, $\pm$) are indicated and point to a problem: compared with the means, the standard deviations are too big to fit normal distributions. Generally, if one to two standard deviations are subtracted from the mean, the result becomes below zero, which is not possible. This becomes very obvious with the values for fenpropimorph in 1993 (cf. also Fig. 1). Instead, in Table 3 geometric means of the samples, multiplicative standard deviations, $\times/\div$ (times/divide), and multiplicative standard errors of the means are indicated. This way of describing data will be discussed below.

4 DISCUSSION

4.1 Multiple resistance and its evolution

Important questions both for fundamental and applied research are related to the genetics of fungicide resistance. If the same gene(s) affect the sensitivity to compounds with different modes of action, we speak about cross-resistance that can be positive or negative. For practical reasons, chemicals are grouped according to their cross-resistance behaviour. DMIs show positive cross-resistance,[10,16] as do the morpholines.[11]

No cross-resistance is found between DMIs and morpholines, which means that resistance to the two groups is due to different genes. However, combining these genes can lead to multiple resistance.[2] A main aim of the present investigation was to analyse the extent of multiple resistance to triadimenol (*Rtria*) and to fenpropimorph (*Rfen*) representing the group of DMIs and morpholines, respectively, and its evolution from 1993 to 1996.[14] As the cereal mildews are haploid, the phenotype is supposed to reflect the genotype, and the answer to the question for multiple resistance can be deduced immediately from the phenotypic expression. Two outcomes are possible: the genes can be combined effectively, or not.

In the latter case, if high levels of *Rdmi* and *Rmor* were difficult to combine in the same genotype, the resulting distribution of sensitivity depicted as in Figs 1–4 would be hyperbolic: types exhibiting moderate multiple resistance would form the central curved part of the hyperbola in the lower left of the graphic; the remaining parts of the hyperbola would be formed by types expressing only one or the other resistance to a higher level.

In contrast to that possibility, there was no hyperbolic relation of sensitivity to both chemicals. The sensitivity distribution shown in Figs 1–4 and particularly in the latter two directly indicates the levels of multiple resistance present. As resistance to DMIs and morpholines is controlled by different genes, the sensitivities of the isolates to the representatives of the two groups of chemicals do not need to be correlated. This is in contrast to cross-sensitivity tests involving chemicals of the same group, where correlations are expected to be highly positive, and found to be so.[16]

Instead, for multiple resistance, a further quantitative answer can be obtained from the analysis of covariance that indicates in how far resistance to one chemical changes with resistance to the other. The relationship and evolution observed both from bulk and single colony isolates, compared with the standard isolates representing the original sensitivity of the population, become evident from Fig. 5. The coefficient of covariance of the regression is 0·95, thus indicating a similar degree of resistance to both chemicals. Evolution of multiple resistance was not detected in the Netherlands,[17] which may be due to differences in the methods used,[18] and to the degree of resistance encountered, which was found to be considerably lower in that country at the time of the investigation.

A review of the history of SBI resistance in cereal mildews can offer some further clues to the understanding of the appearance of multiple resistance. *Rdmi* appeared a few years after the release of triadimenol for

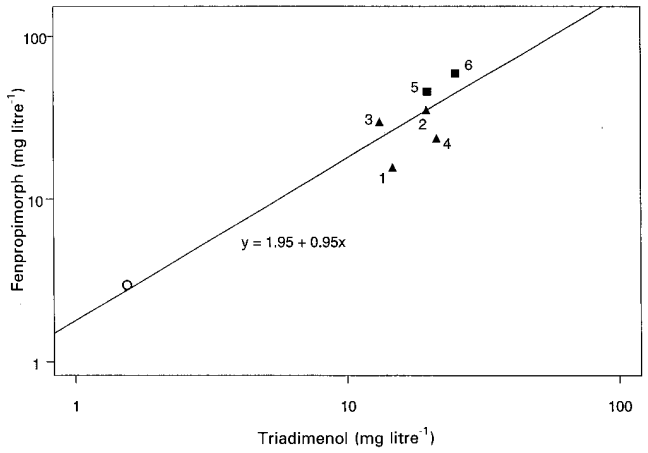

Fig. 5. Evolution of multiple resistance to triadimenol and fenpropimorph from 1993 to 1996. Indicated are mean EC_{50} values of the standard isolates, the bulk samples and the single colony samples from Département Cher, and the regression line. (○) standard isolates; (▲) bulk samples, 1–4 = 1993–1996; (■) single colony samples, 5, 6 = 1994, 1996. The coefficient of covariance of the regression is 0·95.

mildew control.[19,20] As selection due to fungicides, unlike that conferred by host resistance, is restricted to part of the host life, it can be concluded that *Rdmi* appeared after little selection. European surveys showed that sensitivity of the original populations was close to RF 1 and varied little. Their factors of standard deviation were approximately 1·4, which means that 95% of the population was in the range of RF 0·5 to 2 (RF 1 $\times/\div$ $1{\cdot}4^2$) (Limpert, unpublished data and References 21, 22). In contrast, in selected populations from parts of Europe with extensive fungicide use, RFMs to triadimenol in barley mildew have surpassed 400 since the beginning of the 1990s (Limpert, unpublished data, and Reference 23), with data for wheat mildew close to RFM 50.[24,25]

It was only after the appearance of *Rdmi* that first evidence of *Rmor* appeared in barley and wheat mildew pathogens.[22,23,26,27] The changing composition led cereal mildews to be considered as high-risk pathogens for resistance to SBIs.[27] Morpholines were first used in alternation with DMIs, which may have reduced the selection of multiple resistance to the two groups of compounds. However, during the 1990s, mixtures of DMIs and morpholines were increasingly used, combined with increasing selection pressure for multiple resistance in the pathogen.

Possibly, the variation for *Rmor* was reduced in the beginning of selection and, due to both clonal propagation and bottlenecks in the population from one region, the variation of types expressing multiple resistance at high levels was limited. This can be the explanation for the peculiar sensitivity distribution observed in Fig. 3. Apparently, among the group of SCIs in the upper right, the variation of *Rfen* was limited and points to a founder effect, in contrast to the picture two years later (Fig. 4).

Trying to compare the data on the evolution of multiple resistance with data on selection in France, we are grateful to A. Paturel (AgrEvo) for the information on DMI and morpholine use. As mildew sampling was done each year in March before the first treatment, the fungicide use corresponding to the three-year period of investigation (1993–1996) is that from 1992 to 1995 (Table 4). Whereas the DMI use on winter wheat increased during that period from 1·62 to 1·92, that of morpholines decreased from 0·84 to 0·52.

The evolution of resistance described in these studies is in some contrast with this pattern of use. The RFM for *Rtria* had increased from 9·59 in 1993 to close to 14 at the end of the investigation, and that of *Rfen* from 5·11 to close to 8, respectively. In both cases resistance increased by close to 150% compared with an increase in DMIs use of 118·5% only and, surprisingly, a decrease of morpholine use to 61·9%.

4.2 Distribution of fungicide sensitivity

There is a need for closer consideration of the distribution of fungicide sensitivity in the population and, in particular, for improvements of statistical description of the data. The problem shown in Table 2 is caused by the asymmetric, skewed and non-Gaussian distribution of sensitivity which is not normal but, rather, lognormal. Therefore, the way of describing normal distributions by the *arithmetic* mean and the *additive* ($\pm$) standard deviation is not appropriate, above all due to the risk of misunderstanding the genetic potential for resistance in the pathogen population.

Sensitivity data are increasingly recognised to be lognormally distributed.[16,28,29] However, such data often continue to be presented, inadequately, as normal distributions, which leads to values as in our Table 2. For instance, the sensitivity of field isolates of *Botrytis cinerea* Pers. ex Fr. to triadimenol was described by a mean EC_{50} of $4{\cdot}1(\pm 3{\cdot}7)$ μg ml^{-1}.[28] A closer look at these results reveals the disadvantages associated with this way of description. About two-thirds of the isolates fell below the mean, but, nevertheless, the distance to the most sensitive isolate was one standard deviation (SD) only. In contrast, the most resistant isolate was as far as 7·7 SD above the mean. This way of description makes recognition of the underlying principles and of the genetic potential of the pathogen difficult. Another important measure in studies of fungicide resistance is lesion size, which also appears to be lognormally distributed (Limpert, unpublished) and was described with an average size of e.g. $78(\pm 59)$ mm^2.[16] A further way of description is nonparametric, by giving the 95% confidence intervals. This approach, however, needs extensive tables[29] and, possibly more important, hides information on the variance parameter that can be valuable for assessment of resistance risk (Limpert and Stahel, unpublished).

To eliminate these problems we propose an easy way to characterise lognormal distributions: the original values are transformed to logarithms, from which the two parameters, mean and standard deviation, are calculated as for normal distributions. Back-transforming the latter values, i.e. building their anti-logs, will give the geometric mean and the multiplicative (times/divide, $\times/\div$) standard deviation. In Table 3 we give the standard error of the mean, which is obtained dividing the standard deviation, before back-transforming, by the square root of sample size ($\sqrt{n}$). For triadimenol in 1993 the mean was 14·7 and its standard error $\times/\div 1{\cdot}09$, which means that the 68% confidence interval is from 13·5 to 16, and the 95% interval from 12·4 to 17·5 ($14{\cdot}8 \times/\div 1{\cdot}09^2$).

5 CONCLUSIONS AND OUTLOOK

5.1 Fungicide resistance

5.1.1 Multiple resistance

The potential of the pathogen to overcome more than one measure of control due to recombination of the respective genes has long been a topic of concern in respect to pathogen virulence against genes conferring resistance in the host.[7–9,13] From this view, it is surprising that multiple resistance of cereal mildews to the major fungicides, which is important for resistance management, has not been considered in more detail before. Multiple resistance of *Botrytis cinerea* in French vineyards is evident to carbendazim, diethofencarb and dicarboximides.[30,31] In the French wheat mildew population, an increase of resistance to DMIs and morpholines was evident from 1993 to 1996, which could be attributed mainly to the evolution of multiple resistance. Multiple resistance was proved with the analysis of SCIs, but bulk tests gave similar results, which means that the latter, less time-consuming way of investigation is also suited for its analysis.

5.1.2 Comparison with fungicide use

The 1993 data suggest evolution of multiple resistance to have started already before that time, which is not surprising from the preceeding history. In contrast to expectation, however, the decreasing use of morpholines after 1992 correlates with increasing morpholine resistance. This is particularly remarkable, as selection in recent years was mostly due to the favoured use of mixtures of DMIs and morpholines. Evidently, mixtures of fungicides do not leave much possibility for the fungus to escape selection to one or the other compound. Probably, however, once multiple resistance has evolved and the use of one compound decreases, fungicide mixtures favour further increase in resistance to that compound or its persistance at a high level. In comparison, separate use of the compounds would select independently from each other. Unfortunately, sufficient data on the proportion of these fungicides used as mixtures or separately are not available to allow that point to be examined further. Such data need to be made available for future studies.

TABLE 4
Development of Fungicide Use in Winter Wheat in France from 1992 to 1995

			1992	*1993*	*1994*	*1995*
DMIs	Applications	(no.)	1·62	1·64	1·81	1·92
		(%)	100	101·2	111·7	118·5
Morpholines	Applications	(no.)	0·84	0·73	0·57	0·52
		(%)	100	86·9	67·9	61·9

5.1.3 Importance of quantitative resistance

As the degree of fungicide resistance varies, the term needs to be treated quantitatively. Whereas in 1993 the RFM of the French wheat mildew population to triadimenol was close to 10 and to fenpropimorph close to 5, it increased up to 14 and 8, respectively, at the end of the investigation. These levels of resistance are enough to considerably impair mildew control in the field. Resistance factors of 2 to 4 to dodine in the apple scab fungus, *Venturia inaequalis* (Cooke) Winter, were sufficient to make the use of this fungicide uneconomic.[32]

In general, low resistance factors are particularly important for two reasons related to exponential changes with time. One relates to the decrease of concentration of the active compound after application, the other to the increase of biomass produced. Thus, if RF 100 would allow the pathogen to overcome the treatment immediately after application, RF 10 can be sufficient to allow fungus development during most of the time on 80% or more of the biomass that should be protected. This has been demonstrated in more detail elsewhere,[21] based on data of the exponential decrease of [^{14}C]triadimenol.[33]

5.1.4 Considering the future of fungicide use

Our results show a need for further ways of fungus control. Promising chemicals appear to be the strobilurins, quinoxyfen and cyprodinil, as well as compounds conferring systemic acquired resistance.[34–37] Fungicide mixtures seem to continue to be favoured on the market, but how they interfere with resistance build-up depends, in addition to the points made, on some points that need to be clearly recognised. Fungicides with negative cross-resistance would be ideally suited for mixtures. However, in contrast to the many cases reported of cross-resistance being positive or absent, cases of negative cross-resistance are rare in practice. Mixtures of compounds affecting the same biochemical pathway via different modes of action are also useful. Although this holds for the DMIs and morpholines, the

latter were introduced too late as mixture components as the former had already been overcome by the pathogen.

5.2 Further prospects

5.2.1 Recognising multiplicative interactions

There is an increasing need for improved understanding of multiplicative, lognormal interactions, which seems invaluable for assessment of resistance risk. To this aim, a 'log-Galton board' was developed that is able to model lognormal distributions (Limpert, unpublished), as the Galton board does for normal distributions.[38] Together with additional considerations of the multiplicative standard deviation (Limpert and Stahel, unpublished) it is intended to provide new keys and clues for an improved understanding of the lognormal distribution that should also help to fill present gaps of knowledge of the genetic part of variation of fungicide sensitivity at the population level.[39]

5.2.2 New technologies

New tools with immuno- or DNA-based technologies will provide a deeper understanding of the composition of pathogen populations and their evolution. For instance, sequencing the gene encoding the target enzyme of DMIs against *Uncinula necator* (Schw)Burr., powdery mildew on grape, allows the investigation of mutations that confer DMI resistance.[40] It would be challenging to adapt the procedure to the cereal mildews that are among the pathogens for which the population genetics of host–pathogen interactions is well documented from the field to the European level.[8,9]

Improved knowledge of population genetics, combined with improved use of chemicals as well as host resistance as another main factor in integrated disease management[41–44] may make the size and variability of the pathogen population decline and, in consequence, lose its capacity for rapid adaptation to control measures.

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